

Baroreceptor unloading does not limit forearm sweat rate during severe passive heat stress.

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Abstract

This study tested the hypothesis that sweat rate during passive heat stress is limited by baroreceptor unloading associated with heat stress. Two protocols were performed in which healthy subjects underwent passive heat stress that elicited an increase in intestinal temperature of $\sim 1.8^{\circ}\text{C}$. Upon attaining this level of hyperthermia, in *protocol one* ($n=10$, 3 females) a bolus (19 ml/kg) of warm ($\sim 38^{\circ}\text{C}$) isotonic saline was rapidly (5-10 min) infused intravenously to elevate central venous pressure (CVP), while in *protocol two* ($n=11$, 5 females) phenylephrine was infused intravenously (60-120 $\mu\text{g}/\text{min}$) to return mean arterial pressure (MAP) to normothermic levels. *Protocol one*: Heat stress reduced CVP from 3.9 ± 1.9 mmHg (normothermia) to -0.6 ± 1.4 mmHg ($P<0.001$), while saline infusion returned CVP to normothermic levels (5.1 ± 1.7 mmHg; $P>0.999$). Sweat rate was elevated by heat stress (1.21 ± 0.44 mg/cm²/min) but remained unchanged during rapid saline infusion (1.26 ± 0.47 mg/cm²/min, $P=0.5$), whereas CVC increased from 77 ± 10 to $101 \pm 20\%$ of local heating max ($P=0.029$). *Protocol two*: MAP was reduced with heat stress from 85 ± 7 mmHg to 76 ± 8 mmHg ($P=0.048$). Although phenylephrine infusion returned MAP to normothermic levels (88 ± 7 mmHg; $P>0.999$), sweat rate remained unchanged during phenylephrine infusion (1.39 ± 0.22 mg/cm²/min vs. 1.41 ± 0.24 mg/cm²/min; $P>0.999$). These data indicate that both cardiopulmonary and arterial baroreceptor unloading do not limit increases in sweat rate during passive heat stress.

Keywords: Arterial baroreceptors; Cardiopulmonary baroreceptors; Hyperthermia; Central venous pressure; Skin blood flow; Sweat rate.

INTRODUCTION

Sweating and cutaneous vasodilation are elicited not only by increases in core and skin temperatures, but also by non-thermal factors. For instance, central command, metaboreceptors, mechanoreceptors, and osmoreceptors all independently affect *both* sweating and cutaneous vasodilation (20, 23). In contrast, baroreceptors have long been known to influence cutaneous vasodilation (11), but their influence upon sweat rate remains debatable (31).

Passive heat stress reduces cardiac filling pressures (38) and arterial blood pressure (7), unloading both cardiopulmonary and arterial baroreceptors respectively. The vast majority of studies examining a potential role for baroreceptors in the control of sweating during passive heat stress have done so using perturbations that further unload baroreceptors. Such studies, using passive heat stress in combination with either head-up tilt (37), pharmacological agents (36), or during lower body negative pressure (1, 24), have consistently shown that further baroreceptor unloading does not affect sweat rate or its thermal sensitivity. In contrast, baroreceptor unloading modulates sweat rate during the recovery from dynamic exercise (19), which is also characterized by a state of arterial and cardiopulmonary baroreceptor unloading, as cardiac filling and arterial blood pressures are reduced (9, 10). Rather than eliciting further baroreceptor unloading, however, post-exercise studies have shown that arterial and/or cardiopulmonary baroreceptor “reloading” maintains sweat rate at elevated levels, particularly during the early stages of recovery following dynamic exercise (13-15, 17, 28). It is therefore conceivable that the discrepancy between passive heat stress and post-exercise studies regarding the potential role of baroreceptors in modulating sweat rate results from the former relying on procedures that cause further baroreceptor unloading (e.g., lower body negative pressure, head-up tilt, pharmacological reductions in blood pressure), whereas the latter relied upon maneuvers that cause baroreceptor reloading (e.g. lower body positive pressure, head-down tilt, supine posture).

Few studies have attempted to examine whether baroreceptor reloading can influence sweat rate during passive heat stress. Our laboratory has previously shown that brief sequential decreases and increases in mean arterial pressure do not cause parallel changes in sweat rate in passively heat stressed subjects (36). Furthermore, sweat rate is unaffected during passive heating performed in a head-down tilt position relative to the upright seated posture (18). However, findings from both studies are limited in that arterial baroreceptor

reloading was very brief (<1 min) and immediately followed sodium nitroprusside infusion and subsequent arterial baroreceptor unloading (36), while head-down tilt did not fully offset baroreceptor unloading associated with heat stress (18). As such, it remains to be determined whether baroreceptor unloading during heat stress limits the increase in sweat rate and if so, whether one baroreceptor population (arterial vs. cardiopulmonary) is primarily responsible. Our laboratory has previously shown that cardiopulmonary baroreceptor reloading via rapid saline infusion allows for greater increases in cutaneous vasodilation during passive heat stress (3). These findings suggest that cardiopulmonary baroreceptor unloading limits the increase in cutaneous vasodilation during passive heat stress in humans. Therefore, the purpose of this study was to examine whether baroreceptor unloading also limits the increase in sweat rate during passive heat stress. We also examined potential separate influences of cardiopulmonary and arterial baroreceptors by performing procedures that primarily targeted each population. We tested the hypothesis that both cardiopulmonary and arterial baroreceptor unloading limit the increase in sweat rate during passive heat stress, such that reloading both baroreceptor populations would further elevate sweat rate.

METHODS

Two protocols were undertaken. Ten subjects (3 females) participated in *protocol one*, while 11 subjects (5 females) participated in *protocol two*. Subject characteristics (mean \pm SD) for *protocol one* were: age, 29 ± 5 y; height, 177 ± 10 cm; weight: 75.5 ± 12.2 kg and for *protocol two* were: age, 26 ± 5 y; height, 178 ± 12 cm; weight: 71.3 ± 14.9 kg. Subjects were non-smokers, not taking medications, and were free of any known cardiovascular, metabolic, neurological, or psychological diseases. Since only within subject comparisons were performed in the current study (see statistical analysis section), menstrual cycle phase was recorded but not controlled for in female subjects. Each subject was fully informed of the experimental procedures and possible risks before giving informed, written consent. Both protocols and the informed consent were approved by the Institutional Review Boards at the University of Texas Southwestern Medical Center at Dallas and Texas Health Presbyterian Hospital of Dallas, and all procedures conformed to the standards set by the Declaration of Helsinki. Subjects arrived at the laboratory euhydrated, confirmed via urine specific gravity (*protocol one*: 1.015 ± 0.008 ,

117 *protocol two*: 1.012 ± 0.008), and were asked to refrain from strenuous exercise, alcohol and
118 caffeine for a period of 24h prior to their arrival.

120 **Instrumentation**

121 *Both protocols*: Approximately 120 min prior to experimental testing, each subject
122 swallowed a telemetry pill (HQ Inc., Palmetto, FL, USA) for the measurement of intestinal
123 temperature. Mean skin temperature was measured as the weighted average of six
124 thermocouples (abdomen, calf, chest, lower back, thigh, upper back) attached to the skin (34).
125 Mean body temperature was subsequently calculated as: intestinal temperature $\times 0.8$ + mean
126 skin temperature $\times 0.2$. Body temperature was controlled via a water-perfused tube lined suit
127 (Med-Eng, Ottawa, ON, Canada) that covered the entire body except the head, hands, one
128 forearm, and the feet. Blankets were placed on the subjects to minimize any potential heat loss
129 from sweat evaporation. Heart rate was continuously recorded from an electrocardiogram (HP
130 Patient Monitor, Agilent, Santa Clara, CA, USA) interfaced with a cardiometer (CWE,
131 Ardmore, PA, USA). Beat-to-beat blood pressure was measured continuously via the Penaz
132 method (Finometer Pro, FMS, Amsterdam, The Netherlands), which was confirmed
133 intermittently via auscultation of the brachial artery by electrospigmomanometry (Tango+,
134 SunTech, Raleigh, NC, USA). Forearm (local) sweat rate was measured by placing a plastic
135 capsule covering 2.83 cm^2 of skin on the ventral surface of the exposed forearm. This capsule
136 was perfused with dry nitrogen at a flow rate of 0.3 L/min. Water vapor in the gas exiting the
137 capsule was measured by capacitance hygrometry (Vaisala, Woburn, WA, USA), and forearm
138 sweat rate was calculated by multiplying the humidity output (in g/m^3) by flow rate and dividing
139 that value by the surface area of the capsule.

141 *Instrumentation unique to protocol one*: Skin blood flow was measured via laser-Doppler
142 flowmetry (Periflux System 5000, Perimed, Stockholm, Sweden) from the ventral surface of the
143 uncovered forearm. At the end of the experimental protocol, the area surrounding the laser-
144 Doppler probe was heated to 44°C for 30 minutes to produce a locally induced maximum skin
145 blood flow (16). Cutaneous vascular conductance was calculated as laser-Doppler flux divided
146 by mean arterial pressure and expressed as a percentage of maximum. In 8 of 10 subjects, a
147 peripherally inserted central venous catheter was advanced into the superior vena cava via the
148 basilic vein. Positioning of the central venous catheter was confirmed by: 1) the distance that

the catheter was advanced, 2) observation of adequate pressure waveforms, and 3) an appropriate rapid rise and fall in pressure during a Valsalva and Mueller maneuver, respectively. The central venous catheter was connected to a pressure transducer and zeroed at the position of the midaxillary line. This catheter was used for continuous measurement of central venous pressure (CVP).

Experimental protocol one

This protocol was performed to determine whether reloading of primarily the cardiopulmonary baroreceptors, via restoring hyperthermia-induced reductions in CVP to normothermic levels, increased sweat rate during passive heat stress. Following instrumentation, subjects rested in the supine position for a minimum of 30 min, while 34°C water circulated through the suit, after which baseline normothermic thermal and hemodynamic data were obtained. Subjects were then passively heated by circulating ~49°C water through the suit. After intestinal temperature increased ~1.8°C, warmed (~38°C) isotonic saline was rapidly administered over 6.9 ± 2.1 min through a catheter placed in an antecubital vein (different from the one used to place the CVP catheter) sufficient to return CVP to pre-heat stress levels (2, 3). After the infusion, mean skin temperature was returned to pre-heat stress levels by perfusing the suit with cool (~20°C) water during which time maximum skin blood flow was determined by local heating.

Experimental protocol two

This protocol was performed to determine whether reloading of primarily arterial baroreceptors, via restoring hyperthermia-induced reductions in mean arterial pressure (MAP) to normothermic levels, increased sweat rate during passive heat stress. Similar to protocol one, subjects rested in the supine position following instrumentation but their lower legs were suspended below heart level (legs were bent at knees at ~73° angle), promoting reductions in MAP during passive heat stress. Following a minimum of 30 min, during which time 34°C water circulated through the suit, baseline normothermic thermal and hemodynamic data were obtained. Subjects were then passively heated by circulating ~49°C water through the suit. After intestinal temperature increased ~1.8°C, phenylephrine (60–120 µg/min) was intravenously titrated for 5 min to increase MAP 12 ± 3 mmHg, restoring MAP to normothermic

levels. Skin blood flow was not measured in this protocol as phenylephrine acts directly on the cutaneous vasculature, independent of neural control.

Data and statistical analyses

Data were acquired continuously at 50 Hz throughout the experiment (Biopac, Santa Barbara, CA, USA). Data are presented as a 1 min average immediately before whole-body heating (normothermia) and immediately before rapid saline (*protocol one*) or phenylephrine (*protocol two*) infusion (hyperthermia), while data throughout the saline and phenylephrine infusions are presented as minute averages. The duration of the saline infusion differed between subjects (range: 5 – 10 min). Therefore, the first 4 min of these data, and data during the final minute of the infusion, are presented. All data were statistically analyzed using one-way repeated-measures analysis of variance with the repeated factor of time (normothermia, hyperthermia, as well as min 1-4 and the final min, or min 1 through 5 of rapid saline and phenylephrine infusions, respectively), and where appropriate, *post hoc* Bonferroni pair-wise comparisons were made. Data were analyzed using GraphPad Prism (version 6, GraphPad Software, Inc., La Jolla, CA, USA) with *a priori* statistical significance set at $P \leq 0.05$. All data are reported as mean \pm SD.

RESULTS

Protocol one

Passive heat stress increased intestinal temperature, mean skin temperature, and heart rate (all $P < 0.001$), while MAP was unchanged ($P = 0.765$, Table 1). CVP decreased ($P < 0.001$) with heat stress, while forearm sweat rate and CVC were increased ($P < 0.001$, Figure 1). Rapid infusion of 19 ± 2 ml/kg of saline raised CVP ($P \leq 0.019$), returning it to normothermic values ($P > 0.999$, Figure 1). This saline infusion caused further increases in CVC ($P \leq 0.051$), but did not cause any further changes in forearm sweat rate ($P \geq 0.439$, Figure 1). By the end of the saline infusion, intestinal temperature had further increased by $0.2 \pm 0.1^\circ\text{C}$ ($P = 0.005$), while MAP decreased to values that were lower than during normothermia ($P = 0.029$, Table 1).

Protocol two

Passive heat stress increased ($P < 0.001$) intestinal temperature, mean skin temperature, heart rate, and forearm sweat rate (Table 2, Figure 2), while MAP decreased by 9 ± 7 mmHg

($P=0.048$, Figure 2). Phenylephrine infusion increased MAP ($P<0.001$), restoring it to normothermic values ($P>0.999$), but did not affect forearm sweat rate ($P>0.999$, Figure 2). By the end of the phenylephrine infusion, intestinal temperature had further increased by $0.2 \pm 0.1^{\circ}\text{C}$ ($P<0.001$), while heart rate decreased ($P<0.001$) relative to that occurring during hyperthermia (Table 2).

DISCUSSION

This study tested the hypothesis that baroreceptor unloading associated with passive heat stress limits the increase in sweat rate. Contrary to our hypothesis, reloading of primarily cardiopulmonary (via rapid saline infusion) and primarily arterial (via phenylephrine infusion) baroreceptors did not elicit further increases in sweat rate (Figures 1 and 2). Therefore, the current results suggest that baroreceptor unloading coincident with severe passive heat stress does not limit increases in sweat rate during this exposure in humans.

A number of studies have examined a potential role for baroreceptors in modulating sweat rate during exercise, passive heat stress, and during the recovery from dynamic exercise. Findings from early studies comparing thermoregulatory responses during supine (i.e. baroreceptor loading) and upright (i.e. baroreceptor unloading) exercise suggest that baroreceptor unloading during exercise does not affect sweat production (8, 21), but that upright exercise delays the onset threshold for cutaneous vasodilation (12, 29). Subsequently, studies using lower body negative pressure established a potential role for cardiopulmonary baroreceptor unloading in altering the neural drive (i.e. skin sympathetic nerve activity) for sweating (5) as well as both the onset threshold for sweat production (27) and its sensitivity to changes in core temperature (26, 32). These latter findings, however, were largely attributed to potential reductions in skin temperature that accompany the use of lower body negative pressure (35), which can decrease sweat rate independent of baroreceptor unloading (39). Consequently, a number of studies using alternative methods to unload baroreceptors, while minimizing decreases in skin temperature, were undertaken. In these studies, passive heat stress in combination with either head-up tilt (37), pharmacological agents (36), or during lower body negative pressure with or without small decreases in skin temperature (1, 4, 24) have consistently shown that further baroreceptor unloading (relative to that which occurs during

heat stress itself) does not affect skin sympathetic nerve activity, sweat rate or its thermal sensitivity.

In contrast to passive heat stress studies, baroreceptor modulation of sweating has consistently been demonstrated during the recovery from dynamic exercise. Rather than eliciting further baroreceptor unloading, as in the aforementioned passive heat stress studies, most of these studies reversed the cardiopulmonary and/or arterial baroreceptor unloading that typically occurs post-exercise (9, 10). For example, Journeay *et al.* (14) used lower body positive pressure to reload cardiopulmonary and arterial baroreceptors following dynamic exercise and observed elevated sweat rates that ultimately resulted in a faster return of core temperature to baseline compared to a control (i.e., no positive pressure) condition. Similarly, a number of other post-exercise studies have shown that baroreceptor reloading maintains sweat rate at elevated levels compared to when baroreceptors are naturally unloaded during inactive recovery following dynamic exercise (13, 15, 17, 28). In light of the findings from these studies, we hypothesized that the cardiopulmonary and arterial baroreceptor unloading which occurs during passive heat stress places a “brake” on sweat rate. If so, then releasing that figurative brake, by returning the loading status of these baroreceptors to pre-heat stress levels, would elicit further increases in sweat rate. Contrary to this hypothesis, however, sweat rate remained unchanged during both rapid saline (Figure 1) and phenylephrine (Figure 2) infusions. In contrast, and as previously shown (3), cardiopulmonary baroreceptor reloading via rapid saline infusion elicited large increases in cutaneous vascular conductance (upwards of 25%; Figure 1). It should be considered that small decreases in MAP (i.e., arterial baroreceptor unloading) during rapid saline infusion may have negated potential increases in sweat rate during reloading of cardiopulmonary baroreceptors. However, a targeted reloading of arterial baroreceptors via phenylephrine infusion had no effect on sweat rate during *protocol two* (Figure 2), suggesting that the lack of increase in sweat rate during rapid saline infusion is not confounded by small decreases in MAP. Overall, the current data suggest that while cardiopulmonary baroreceptor unloading may limit increases in cutaneous vasodilation during passive heating in humans, they do not appear to limit the increase in sweat rate. Furthermore, these observations support prior observations of differential baroreceptor control of skin blood flow and sweating in the passively heat stressed human (12).

276 It should be noted that at least two previous studies have examined the effect of
277 baroreceptor loading on sweat rate during passive heat stress, although definite conclusions
278 as to a potential modulation of sweat rate by baroreceptors could not be reached. Our
279 laboratory previously reported that sweat rate during passive heat stress was unaffected by
280 bolus infusions of sodium nitroprusside immediately followed by phenylephrine that elicited
281 sequential decreases and increases in blood pressure (36). Although these findings suggested
282 that arterial baroreceptor loading does not affect sweat rate during passive heat stress, no
283 insight into a potential role for cardiopulmonary baroreceptor loading could be assessed.
284 Moreover, conclusions regarding arterial baroreceptor control of sweating from that study are
285 clouded by the fact that: 1) in all cases, blood pressure was first reduced by sodium
286 nitroprusside, which likely affected the extent of arterial baroreceptor reloading during
287 subsequent phenylephrine administration, and 2) the short period of time blood pressure was
288 elevated (typically <1 min) as a result of the bolus approach, which may have been insufficient
289 to observe any effects upon sweat rate. Furthermore, Kenny *et al.* (18) compared sweating and
290 cutaneous vascular conductance during passive heat stress in the upright seated position
291 (baroreceptor unloading) and during 15° head-down tilt (baroreceptor loading). Although they
292 did not observe any differences in either sweating or cutaneous vascular conductance
293 between conditions, it is possible that 15° head-down tilt was not sufficient to fully reload
294 baroreceptors, as it did not return blood pressure to normothermic levels during the passive
295 heat stress period. Furthermore, 15° head-down tilt did not increase cutaneous vascular
296 conductance, despite cardiopulmonary baroreceptor reloading being clearly capable of eliciting
297 further increases in cutaneous vascular conductance [(3), and Figure 1]. Overall, however, the
298 findings of the current study support these previous observations, and extend them by
299 providing conclusive evidence that reloading of either cardiopulmonary or arterial
300 baroreceptors does not affect sweat rate during passive heat stress in humans.

301

302 *Considerations.* The findings of the current study are partly dependent upon the
303 assumption that sweat rate could be further elevated during rapid saline and phenylephrine
304 infusion periods. Considering that core temperature increased ~1.8°C during passive heating,
305 it is possible that any influence of baroreceptor unloading may have been overridden by the
306 high thermal drive. Indeed, previous studies have shown that the relative influence of non-
307 thermal factors, including baroreceptors, is attenuated when thermal drive is elevated (6, 22).
308 Furthermore, maximal levels of forearm sweat rate may have been attained during the heating

period. Both possibilities would have created a “ceiling effect” thus limiting any further increases in sweat rate during baroreceptor reloading. While these considerations may have limited the potential to observe further increases in forearm sweat rate during the baroreceptor reloading periods, their possible occurrence would nonetheless suggest that baroreceptor unloading did not limit the increase in sweat rate during severe passive heating in the current study. If baroreceptor unloading associated with heat stress modulates sweat rate, we would have expected the thermal drive to be insufficient to override this baroreflex influence, which would have effectively limited the increase in sweat rate. This scenario would have provided a background against which to observe further increases in forearm sweat rate during baroreceptor reloading. Therefore, the lack of increase in forearm sweat rate during both rapid saline and phenylephrine infusions indicates that baroreceptor unloading during severe passive heating did not impede increases in forearm sweat rate. That said, although forearm sweat rate is representative of other non-glabrous areas during passive heating (33) and it responds to non-thermal stimuli similarly to other non-glabrous skin sites (25), we cannot rule out the possibility that sweat rate in other areas of the body increased during the baroreceptor reloading interventions.

Perspectives. The findings from the current study add to a growing body of recent literature indicating that baroreceptors do not influence sweat production during passive heat stress (1, 4, 24, 36, 37). A consistent lack of baroreceptor modulation of sweat production during passive heat stress is puzzling compared to baroreceptor modulation of sweating during (26, 27) and following (13-15, 17, 28) dynamic exercise. Although speculative, it is possible that factors specific to dynamic exercise engage baroreceptors in the control of sweating. Future studies should consider examining this possibility. Determining whether baroreceptors modulate sweat rate during passive heat stress is important as, from a practical perspective, prolonged sweating in hot environments often leads to dehydration (30), exacerbating baroreceptor unloading. Thus, it is perhaps unsurprising that a number of studies have examined a potential role for baroreceptor unloading in eliciting volume preservation responses, such as reducing sweat production. Such a role for baroreceptors (should it exist) would be advantageous for individuals whose occupational or recreational pursuits render them passively hyperthermic, dehydrated, and at an elevated risk of a hemorrhagic injury that would induce further volume loss (e.g. soldiers, firefighters, miners, etc.). The findings of the

current study not only suggest that baroreceptor unloading during such scenarios does not preserve fluid status secondary to decreasing sweat production, but also that reloading of the baroreceptors is unlikely to improve sweat production and therefore contribute to temperature regulation.

CONCLUSION

The current study examined whether baroreceptor unloading limits the increase in forearm sweat rate and cutaneous vascular conductance during severe passive heat stress. The results show that reloading of cardiopulmonary baroreceptors (via rapid saline infusion) elicits large increases in cutaneous vascular conductance, consistent with prior observations (3), without any effect upon forearm sweat rate. Furthermore, infusion of phenylephrine to reload arterial baroreceptors did not elicit further increases in forearm sweat production. These findings suggest that cardiopulmonary and arterial baroreceptor unloading during severe passive heat stress do not limit increases in sweat rate.

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TABLES

Table 1: Thermal and hemodynamic data during normothermia, hyperthermia (pre-saline infusion), and during the last minute of rapid saline infusion (mean \pm SD).

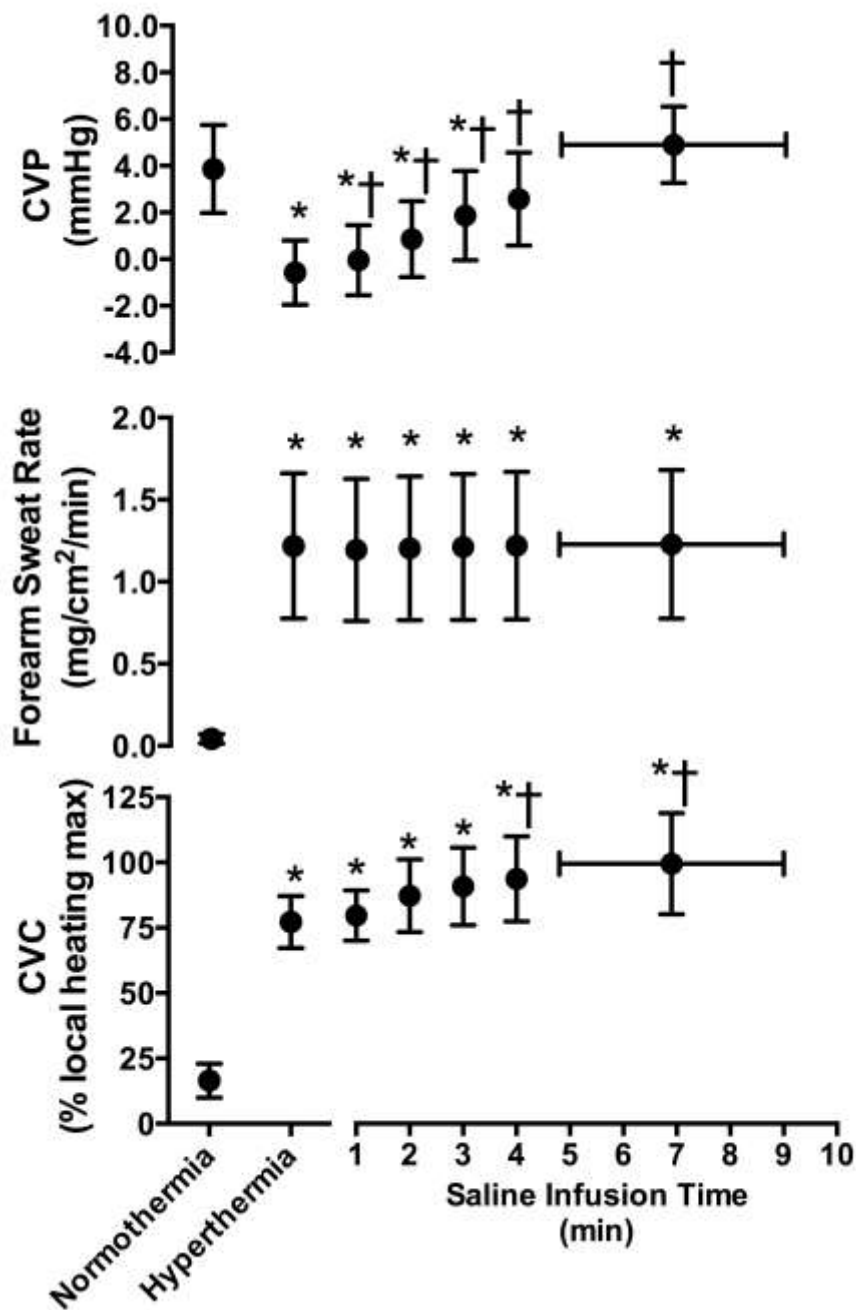
	Normothermia	Hyperthermia	Saline Infusion
Intestinal temperature ($^{\circ}\text{C}$)	37.0 ± 0.3	38.9 ± 0.4 *	39.1 ± 0.5 *†
Mean skin temperature ($^{\circ}\text{C}$)	34.7 ± 0.2	39.3 ± 0.8 *	39.2 ± 0.8 *
Mean body temperature ($^{\circ}\text{C}$)	36.6 ± 0.3	39.0 ± 0.5 *	39.1 ± 0.5 *†
MAP (mmHg)	82 ± 8	79 ± 11	74 ± 8 *
Heart rate (bpm)	59 ± 10	113 ± 17 *	112 ± 14 *

MAP, mean arterial pressure; * Different from normothermia ($P \leq 0.023$); † Different from hyperthermia ($P = 0.005$).

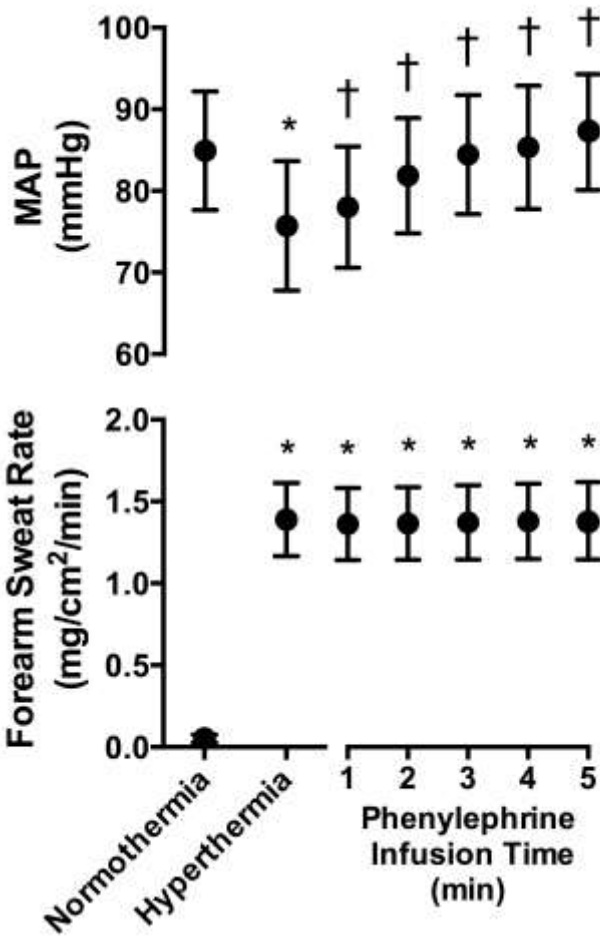
Table 2: Thermal and hemodynamic data during normothermia, hyperthermia (pre-phenylephrine infusion), and during the last minute of phenylephrine infusion (mean \pm SD).

	Normothermia	Hyperthermia	Phenylephrine Infusion
Intestinal temperature ($^{\circ}\text{C}$)	36.9 ± 0.2	38.7 ± 0.4 *	38.9 ± 0.4 *†
Mean skin temperature ($^{\circ}\text{C}$)	33.9 ± 0.5	39.9 ± 0.5 *	39.9 ± 0.4 *
Mean body temperature ($^{\circ}\text{C}$)	36.3 ± 0.2	39.0 ± 0.4 *	39.1 ± 0.4 *†
Heart rate (bpm)	56 ± 9	107 ± 16 *	95 ± 16 *†

* Different from normothermia ($P < 0.001$); † Different from hyperthermia ($P < 0.001$).



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382
383 **Figure 1:** Central venous pressure (CVP, top, n=8), forearm sweat rate (middle, n=10), and cutaneous
384 vascular conductance (CVC, bottom, n=10) immediately prior to passive heat stress (normothermia),
385 during hyperthermia, and throughout the rapid saline infusion (mean ± SD). Data during the infusion are
386 presented until the last common time point of saline infusion (4 min), while the last data point
387 represents the mean infusion time and associated response across all subjects. *Different from
388 normothermia ($P \leq 0.028$); †Different from hyperthermia ($P \leq 0.051$).



390 **Figure 2:** Mean arterial pressure (MAP, top) and forearm sweat rate (bottom) immediately prior to
391 passive heat stress (normothermia), during hyperthermia, and throughout the phenylephrine infusion
392 (mean \pm SD, n=11). *Different from normothermia ($P \leq 0.048$); †Different from hyperthermia ($P \leq 0.007$).
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